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Synthetic retinal analogues modify the spectral and kinetic characteristics of microbial rhodopsin optogenetic tools

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Optogenetic tools have become indispensable in neuroscience to stimulate or inhibit excitable cells by light. Channelrhodopsin-2 (ChR2) variants have been established by mutating the opsin backbone or by mining related algal genomes. As an alternative strategy, we surveyed synthetic retinal analogues combined with microbial rhodopsins for functional and spectral properties, capitalizing on assays in *C. elegans*, HEK cells and larval *Drosophila*. Compared with all-*trans* retinal (ATR), Dimethylamino-retinal (DMAR) shifts the action spectra maxima of ChR2 variants H134R and H134R/T159C from 480 to 520 nm. Moreover, DMAR decelerates the photocycle of ChR2(H134R) and (H134R/T159C), thereby reducing the light intensity required for persistent channel activation. In hyperpolarizing archaerhodopsin-3 and Mac, naphthyl-retinal and thiophene-retinal support activity alike ATR, yet at altered peak wavelengths. Our experiments enable applications of retinal analogues in colour tuning and altering photocycle characteristics of optogenetic tools, thereby increasing the operational light sensitivity of existing cell lines or transgenic animals.

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